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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,924	12/23/2004	Hiltrud Lindenblatt	MERCK-2955	7273
23599	7590	10/24/2006	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			BRADLEY, CHRISTINA	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/518,924	<b>Applicant(s)</b> LINDENBLATT ET AL.	
	<b>Examiner</b> Christina Bradley	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2006.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/23/2004</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> .                 |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. The election of species requirement mailed on 07/28/2006 is withdrawn.

### ***Sequence Compliance***

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2).

However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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5. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jonczyk *et al.* (U.S. Patent No. 6,001,961, Information Disclosure Statement Citation No. 001) in view of Muller *et al.* (WO 85/02767, Information Disclosure Statement Citation No. 004) and Vasudevan *et al.* (WO 00/62793, Information Disclosure Statement Citation No. 005). Jonczyk *et al.* teach oligopeptides of formula I (see abstract) including the specific embodiment cilengitide or cyclo-(Arg-Gly-Asp-DPhe-NmeVal) (see column 13, Example 3). Jonczyk *et al.* do not teach compositions comprising these oligopeptides and an etherified  $\beta$ -cyclodextrin. Muller *et al.* teach aqueous composition comprising a drug and a partially etherified  $\beta$ -cyclodextrins having a water-solubility of more than 1.8 g in 100 ml of water (see page 3, line 30). Vasudevan *et al.* teach compositions of a cyclic oligopeptide-based drug and partially etherified cyclodextrins.

6. It would have been obvious to one of ordinary skill in the art to combine the oligopeptides taught by Jonczyk *et al.* and the etherified cyclodextrin taught by Muller *et al.* The resulting composition would satisfy all of the limitations of claims 1, 2, 7, 13 and 18. Muller *et al.* teach that the ether substituents in the etherified  $\beta$ -cyclodextrin are hydroxymethyl or hydroxypropyl (see page 3, lines 33-36), satisfying claims 3 and 16. Muller *et al.* teach that the etherified  $\beta$ -cyclodextrin has molar degree of substitution between 0.05 and 10, preferably between 0.2 and 2 or 0.25 and 1 (see page 4, lines 22-27), satisfying claims 4-6 and 17. Muller *et al.* teach that the compositions can further comprise sodium chloride, potassium nitrate, glucose, manitole, sorbitol, xylitol or buffers such as phosphate, acetate or citrate, satisfying claims 8 and 19-21. Muller *et al.* teach that the pH of the composition is 6.6, satisfying claims 9, 10, 14 and 15. Muller *et al.* teach that the molar ratio of the drug to cyclodextrin is 1:6 to 4:1, and that generally the drug is added in molar excess relative to the cyclodextrin (see page 5, lines

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1-4), satisfying claims 11 and 12. Vasudevan *et al.* teach compositions of a cyclic oligopeptide-based drug and partially etherified cyclodextrins in which the buffer concentration is 50 mM (see page 22, line 22), satisfying claim 22. Regarding claim 23, the references do not teach the osmolality of the compositions but because the chemical structure of the compositions taught by the combined references are identical to the claimed invention, there is a reasonable expectation that the species would meet this additional limitation. Examiner cannot however determine whether or not the compositions would inherently possess properties which anticipate or render obvious the claimed invention but has basis for shifting the burden of proof to applicant as in *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980). See MPEP § 2112.

7. The skilled artisan would have been motivated to make these compositions as a result of the teaching of Muller *et al.* that hydroxypropyl  $\beta$ -cyclodextrin and other partially etherified cyclodextrins can improve the solubility and stability of drugs. There would have been a reasonable expectation of success given that Vasudevan *et al.* teach such compositions comprising hydroxypropyl  $\beta$ -cyclodextrins and cyclic oligopeptide-based drugs (see page 3). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Bradley whose telephone number is (571) 272-9044.


The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M.

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10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

cmb

  
Cecilia J. Tsang  
Supervisory Patent Examiner  
Technology Center 1600

<b>Notice to Comply</b>	<b>Application No.</b> 10/518,924	<b>Applicant(s)</b> Lindenblatt et al.	
	<b>Examiner</b> Christina M. Bradley	<b>Art Unit</b> 1654	

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS  
CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE  
DISCLOSURES**

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: Pages 2 and 6 of the specification and claim 18 recite sequences greater than 4 amino acids that do not have a SEQ ID NO.

**Applicant Must Provide:**

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923

For CRF Submission Help, call (703) 308-4212 or 308-2923

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